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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/338,904	06/23/99	JOHNSON	P 99-40117-US

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DANIEL H GOLUB
REED SMITH SHAW & MCCLAY LLP
2500 ONE LIBERTY PLACE
1650 MARKET STREET
PHILADELPHIA PA 19103-7301

EXAMINER	
LUNDGREN, J	
ART UNIT	PAPER NUMBER
1631	4

DATE MAILED: 02/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/338,904	Applicant(s) JOHNSON, PETER C.	
	Examiner Jeffrey S. Lundgren	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *12 September 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 (and dependent claims 2-102), and 103 (and dependent claims 104-111) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability of the prior art; (g) the breadth of the claims; and (h) the relative skill in the art.

a) In order to practice the claimed invention (i.e., a method for manufacturing engineered tissue), a first profiling step (i.e., step A), followed by a second design step (i.e., step B), is followed by a manufacturing step for engineering tissue. For the actual

manufacture step, wherein producing an engineered tissue from the aforementioned profile and design steps, would require an unpredictable amount of experimentation from the skilled artisan for the reasons discussed below.

b) While the specification provides guidance (or at least a degree of guidance) for profiling a "normal" tissue specimen, wherein a plurality of structural indices that correspond to statistically significant representations of characteristics of tissue associated with a population, the specification does not provide guidance for manufacturing tissues samples with design characteristics representative of a selected tissue population. Experimental conditions and variables that would produce the designed tissue are not found in the specification.

c) The specification does not provide working examples of a manufacture engineered tissue, wherein the manufactured engineered tissue have been designed in accordance with a profile step.

d) The nature of the invention, which is a method for manufacturing engineered tissue, is complex.

e) The prior art does not teach a method for manufacturing engineered tissues initiated by a profiling step, wherein the profiling step generates a plurality of structural indices followed by a design step, wherein said profiling and design steps establish the necessary experimental conditions for manufacturing an engineered tissue. A plurality of structural indices that correspond to a statistically significant representations of characteristics of tissues from a subset population, wherein the population includes cell

density, matrix density, blood vessel density, and layer thickness, would not be capable of manufacturing engineered tissues with the engineered design.

f) The prior art is unpredictable with regards to methods of manufacturing engineered tissue. Borkenhagen et al. (Journal of Biomedical Research Materials *40*, 392-400, **1998**), disclose a method for manufacturing engineered tissues, and demonstrate that the art of manufacturing engineered tissues is unpredictable. The unpredictability in the art is a result (or partially a result) of the vast number of manufacturing/engineering variables which influence the structural indices of the engineered tissue (see Figures 2-10, and descriptions thereof). The prior art relies on experimentation as a means of determining the proper methods for manufacturing engineered tissues in accordance with a given design.

g) The claims are broad because, claiming a method for manufacturing engineered tissues wherein a step of profiling tissues leads to step of designing tissues in accordance with structural indices, does not enable one of skill in the art with the means to manufacture engineered tissue in accordance with said design.

h) The level of skill in the art of those who practice manufacturing engineered tissues is high.

The skilled practitioner would first turn to the instant specification for guidance in making the manufactured engineered tissue in accordance with engineered tissue design as claimed. However, the specification does not provide sufficient guidance to make the engineered tissue as claimed. As such, the skilled practitioner would turn to

the prior art for such guidance. However, the prior art does not teach the means to manufacture engineered tissue by design from a given profile. Finally, said practitioner would turn to trial and error experimentation to make the manufactured engineered tissue in accordance with design, without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 17, 24, 29, 30, 56-100, and 105-109 are indefinite for reciting the term "normal" in the method of manufacturing engineered tissues. The claim does not set forth the conditions for differentiating between tissues considered "normal", and those that are "abnormal".

Claim 23 is indefinite for reciting the phrase "conforms to a virtual tissue structure" in the method of manufacturing engineered tissues. The claim does not set forth the conditions for differentiating between tissues considered "to conform to virtual tissue", and those that do not "conform to a virtual tissue design".

Claim 27 is indefinite for reciting the phrase "a parameter representative of average cell content" in the method of manufacturing engineered tissues. It is not clear which parameters are representative, or which cell content is average, which Applicant is claiming in the method.

Claim 28 is indefinite for reciting the phrase "a parameter representative of average cell type" in the method of manufacturing engineered tissues. It is not clear which parameters are representative, or which cells are average, which Applicant is claiming in the method.

Claim 50-55, and 110 are indefinite for reciting the phrase "in accordance [with] a correlation" in the method of manufacturing engineered tissues. It is not clear which correlation Applicant is claiming, as correlations are specific mathematical relationships.

Claims 56-100 recites the limitation "the engineered tissue design" in step A of the method of manufacturing engineered tissues. There is insufficient antecedent basis for this limitation in step A of the claim; not until step B is this term introduced.

Claims 101, 102, and 111 are indefinite for reciting the term "common" in the method of manufacturing engineered tissues. The claim does not set forth the conditions for differentiating between features considered "to be common", and those that are "uncommon".

Claims 101, 102, and 111 are indefinite for reciting the phrase "feature that repeats" in the method of manufacturing engineered tissues. The claim does not set forth the conditions for determining the metes and bounds of a "repeating feature".

Conclusion

5. No claims are allowable.

6. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeffrey S. Lundgren whose telephone number is (703) 306-3221. The Examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM (EST), and alternating Fridays from 8:00 AM to 4:30 PM (EST).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Michael Woodward, can be reached at (703) 308-4028.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1631 using (703) 308-0294. Please notify the Examiner of incoming facsimiles prior to sending papers to the aforementioned fax number. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Jeffrey S. Lundgren, Ph.D.

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER